

WHAT IS CLAIMED IS:

1. A *rac*-bicalutamide intermediate having the chemical structure of [X], wherein [X] is a stable organo lithium salt of 4-fluorophenyl methyl sulfone.

5 2. A process of preparing a *rac*-bicalutamide intermediate having the chemical structure of [X], comprising the steps of:

- a) dissolving 4-fluorophenyl methyl sulfone in an organic solvent; and
- b) adding butyl lithium to the solution, wherein butyl lithium reacts with 4-fluorophenyl methyl sulfone to form [X].

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3. The process according to claim 2, wherein the organic solvent is selected from the group consisting of tetrahydrofuran and diethyl ether.

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4. The process according to claim 2, wherein the reaction between butyl lithium with 4-fluorophenyl methyl sulfone occurs in the presence of an anion stabilizer.

5. The process according to claim 4, wherein the anion stabilizer is 1,4-diazabicyclo[2.2.2]octane.

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6. The process according to claim 2, wherein the reaction between butyl lithium with 4-fluorophenyl methyl sulfone occurs in a temperature range between about -40°C to about $+10^{\circ}\text{C}$.

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7. The process according to claim 2, wherein the reaction between butyl lithium with 4-fluorophenyl methyl sulfone occurs in a temperature range between about -2°C and about $+2^{\circ}\text{C}$.

8. A process of preparing ethyl-[2-{4-fluorophenyl sulfone}]-2-hydroxy propionate, comprises the steps of:

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- a) preparing a mixture of 4-fluorophenyl methyl sulfone and butyl lithium in an organic solvent;
- b) adding ethyl pyruvate; and

- c) recovering ethyl-[2-{4-fluorophenyl sulfone}]-2-hydroxy propionate.
9. The process according to claim 8, wherein the organic solvent is tetrahydrofuran.
- 5 10. The process according to claim 8, wherein the ethyl pyruvate is added to the mixture at a temperature of about -65°C .
11. The process according to claim 8, wherein the recovering step comprises evaporating the mixture containing ethyl pyruvate.
- 10 12. The process according to claim 8, wherein the recovering step further comprises separating the ethyl-[2-{4-fluorophenyl sulfone}]-2-hydroxy propionate.
13. A *rac*-bicalutamide intermediate having the chemical structure of [Y], wherein
15 [Y] is a stable organo lithium salt of 5-amino-2-cyano-benzotrifluoride.
14. A process of preparing a *rac*-bicalutamide intermediate having the chemical structure of [Y], comprising the steps of:
- a) dissolving 5-amino-2-cyano-benzotrifluoride in an organic solvent; and
- 20 b) adding butyl lithium to the solution, wherein butyl lithium reacts with 5-amino-2-cyano-benzotrifluoride to form [Y].
15. The process according to claim 14, wherein the organic solvent is selected from the group consisting of tetrahydrofuran and diethyl ether.
- 25 16. The process according to claim 14, wherein the reaction between butyl lithium with 5-amino-2-cyano-benzotrifluoride occurs in the presence of an anion stabilizer.
- 30 17. The process according to claim 16, wherein the anion stabilizer is 1,4-diazabicyclo[2.2.2]octane.

18. The process according to claim 14, wherein the reaction between butyl lithium with 5-amino-2-cyano-benzotrifluoride occurs in a temperature range between about -40°C to about $+10^{\circ}\text{C}$.
- 5 19. The process according to claim 14, wherein the reaction between butyl lithium with 5-amino-2-cyano-benzotrifluoride occurs in a temperature range between about -2°C and about $+2^{\circ}\text{C}$.
20. A process of preparing *rac*-bicalutamide, comprising the steps of:
- 10 a) preparing a mixture of 5-amino-2-cyano-benzotrifluoride and butyl lithium in an organic solvent;
- b) adding ethyl-[2-{4-fluorophenyl sulfone}]-2-hydroxy propionic acid to the mixture; and
- c) recovering *rac*-bicalutamide.
- 15 21. The process according to claim 20, wherein the organic solvent is selected from the group consisting of tetrahydrofuran and diethyl ether.
22. The process according to claim 20, wherein the ethyl-[2-{4-fluorophenyl sulfone}]-2-hydroxy propionic acid is added to the mixture at a temperature of about -65°C .
- 20 23. The process according to claim 20, wherein recovering step comprises evaporating the mixture containing ethyl-[2-{4-fluorophenyl sulfone}]-2-hydroxy propionic acid.
- 25 24. The process according to claim 20, wherein the recovering step further comprises separating the ethyl-[2-{4-fluorophenyl sulfone}]-2-hydroxy propionic acid.
- 30 25. The process according to claim 20, wherein the *rac*-bicalutamide is an R-isomer.
26. The process according to claim 20, wherein the *rac*-bicalutamide is an S-isomer.

27. A process of preparing methyl 1,2-epoxy-2-methyl propionate, comprising the steps of:
- a) dissolving oxone in a basic solution;
 - 5 b) adding methyl methacrylate to the oxone solution;
 - c) adding an acid to the oxone solution to form methyl 1,2-epoxy-2-methyl propionate; and
 - d) recovering methyl 1,2-epoxy-2-methyl propionate.
- 10 28. The process according to claim 27, wherein the basic solution is selected from the group consisting of potassium hydroxide and sodium hydroxide.
29. The process according to claim 28, wherein the potassium hydroxide has a concentration of 10 M.
- 15 30. The process according to claim 27, wherein the oxone is 50% KHSO_5 .
31. The process according to claim 27, wherein the methyl methacrylate is added in methanol.
- 20 32. The process according to claim 27, wherein the oxone solution containing methyl methacrylate is maintained at about pH 6.
33. The process according to claim 27, wherein the acid is selected from the group consisting of hydrochloric acid, nitric acid and phosphoric acid.
- 25 34. The process according to claim 33, wherein the hydrochloric acid has a concentration of about 0.05 N to about 5 N.
- 30 35. A process of preparing 2-hydroxy-2-methyl-3-(4-fluorophenylthio) propionic acid, comprising the steps of:
- a) preparing a solution of 4-fluorothiophenol in methanol;

- b) adding methyl-1,2-epoxy-2-methyl propionate to form a mixture;
- c) adding ethyl acetate to the mixture; and
- d) recovering 2-hydroxy-2-methyl-3-(4-fluorophenylthio) propionic acid.

5 36. The process according to claim 35, wherein the preparation of 4-fluorothiophenol solution is performed by adding a basic solution under N₂ flow.

37. The process according to claim 36, wherein the basic solution is selected from the group consisting of sodium hydroxide and potassium hydroxide.

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38. The process according to claim 37, wherein the sodium hydroxide has a concentration of 2 N.

39. The process according to claim 35, wherein the mixture is formed by stirring.

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40. The process according to claim 39, wherein the stirring is performed at room temperature for 90 minutes.

41. The process according to claim 35, wherein the recovering step is extraction.

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42. The process according to claim 41, wherein the extraction is achieved by chloroform.

43. The process according to claim 35, wherein the recovering step further involves solidifying 2-hydroxy-2-methyl-3-(4-fluorophenylthio) propionic acid.

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44. A micronized *rac*-bicalutamide, wherein the micronized *rac*-bicalutamide has a mean particle diameter of less than about 200 μm.

30 45. A micronized *rac*-bicalutamide, wherein the micronized *rac*-bicalutamide has a mean particle diameter of less than about 100 μm.

46. A micronized *rac*-bicalutamide, wherein the micronized *rac*-bicalutamide has a mean particle diameter of less than 10 μm .
- 5 47. A micronized *rac*-bicalutamide, wherein the micronized *rac*-bicalutamide has a mean particle diameter between about 200 μm to about 10 μm .
48. A pharmaceutical composition of *rac*-bicalutamide comprising a micronized *rac*-bicalutamide and a pharmaceutically acceptable salt.
- 10 49. The pharmaceutical composition of *rac*-bicalutamide wherein the micronized *rac*-bicalutamide has a mean particle diameter between about 200 μm to about 10 μm .